

FDA Plasma Workshop

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- ARC's blood donor recruitment and collection goals are developed with the intent of meeting patients' needs for single donor blood components: red blood cells (particularly group O), platelets, and plasma for transfusion (particularly group AB).
- Plasmapheresis is limited and focused on patients' needs for single unit component transfusion.
- The # of red cell units needed by patients far exceeds the # needed for single donor plasma, so plasma for fractionation is a by product, which optimizes the utilization of the voluntarily donated blood resource, and helps contain the prices for single unit blood components for transfusion (primarily red cells).

Plasma Options

Collection Method	Transfusion	Recovered	Source
Whole Blood	Y	Y	N
Plasmapheresis (= 28 days)	Y	N(*)	(Y)
Plateletpheresis (concurrent plasma)	Y	N(*)	(Y)
# Product Codes	27	9	2
<p>* Only at outdate: 1 year</p> <p>() = ARC does not do, in practice</p>			

Plasma

<u>Product Code</u>	<u>Product Name</u>
18201	Fresh Frozen Plasma
18211	Fresh Frozen Plasma (by pheresis)
18300	Plasma frozen<24hrs after phlebotomy Irradiated
18400	Plasma frozen <24hrs after phlebotomy
18401	Plasma
18411	Plasma (by pheresis)
18435	Plasma Cryoprecipitate Reduced
18451	Plasma Pheresis Frozen within 24 hours
18501	Liquid Plasma
18601	Fresh Frozen Plasma Irradiated
48201	Fresh Frozen Plasma, Divided, Part 1
48202	Fresh Frozen Plasma, Divided, Part 2
48203	Fresh Frozen Plasma, Divided, Part 3
48204	Fresh Frozen Plasma, Divided, Part 4
48205	Fresh Frozen Plasma, Divided, Part 5
48206	Fresh Frozen Plasma, Divided, Part 6
48211	Fresh Frozen Plasma Divided Part 1 (by pheresis)
48212	Fresh Frozen Plasma Divided Part 2 (by pheresis)
48213	Fresh Frozen Plasma Divided Part 3 (by pheresis)
48214	Fresh Frozen Plasma Divided Part 4 (by pheresis)
48215	Fresh Frozen Plasma Divided Part 5 (by pheresis)
48216	Fresh Frozen Plasma Divided Part 6 (by pheresis)
48217	Fresh Frozen Plasma Divided Part 7 (by pheresis)
48218	Fresh Frozen Plasma Divided Part 8 (by pheresis)
48601	Fresh Frozen Plasma Divided Irr Part 1
48602	Fresh Frozen Plasma Divided Irr Part 2
48603	Fresh Frozen Plasma Divided Irr Part 3

Source Plasma

<u>Product Code</u>	<u>Product Name</u>
19711	Source Plasma (by pheresis)
28711	Source Plasma MFG noninjectable

Source Leukocytes/Recovered Plasma/Miscellaneous

<u>Product Code</u>	<u>Product Name</u>
19201	Recovered Plasma MFG Noninjectable
19291	Recovered Plasma Pooled MFG noninjectable
19501	Recovered Plasma Liquid MFG
19591	Recovered Plasma Pooled MFG
19601	Recovered Plasma-Frozen > 24 hrs MFG
19651	Recovered Plasma by Pheresis, MFG
19701	Recovered Plasma-Frozen < 24 Hrs MFG
19801	Recovered Plasma-Frozen within 15 Hrs MFG
20091	Recovered Serum Pooled MFG noninjectable

ARC FY '04 Plasma Production in units

	Collections	Transfusion Plasma	Recovered Plasma	Source Plasma
Whole Blood	6,300,000	1,500,000	4,100,000	N/A
Plasmapheresis (infrequent)	60,000	60,000	N/A	0
Plateletpheresis	400,000	70,000	N/A	0
Total	6, 800,000	1,600,000	4,100,000	0

Whole Blood Collections

- 365 days/year
- 22% collected @ 277 fixed sites
- 78% collected @ >600 different mobile sites each weekday
- Ave. time of collections @ site = 5 hours
- 4.3M available for time-sensitive component manufacture (FFP, Cryo, Platelet Concentrate), using extra component pick up runs
- 2.2 M collected > 120 miles from lab (freezer)
- Future plans include consolidation of # of sites

Group AB Plasma

- Universal donor type for plasma transfusion
- Used in neonates
- 4% US population is AB
- AB FFP is chronically in short supply
- 40% plasmapheresis collections are AB

Plateletpheresis—concurrent plasma

- If can't achieve 2 platelet products/donation, often can collect an extra unit of plasma
- Plasma is a byproduct; frozen within 6 hours of collection
- Provides “jumbo” plasma units
 - Decreases donor exposure for recipient
 - Fewer units for hospital to thaw
 - May take longer to thaw prior to transfusion

Plasma: Time Interval to Freezing After Collection, storage temps, and dating

- FFP (>1M units) & 1st Stage Cryo
 - Freeze w/in 8 hours
 - Store at $< -18^{\circ}\text{C}$; 1 year dating
- Frozen Plasma 24 hours (>400K units)
 - Freeze w/in 24 hours
 - Store at $< -18^{\circ}\text{C}$; 1 year dating
- Recovered Plasma (>4M units)
 - Time interval to freezing after collection specified in contracts with fractionators (3.3M <24hours; 800K >24hours)
 - Store at $< -18^{\circ}\text{C}$ or $< -20^{\circ}\text{C}$ per fractionator; no outdate (fractionators specify 1 or 3 yrs however)

Plasma: Speed of Freezing

Current Status:

- (135) of blast freezers at (35) sites
- Rationale for use
 - Freeze FFP within 6-8 hour limit (incl transportation time)
 - Maximize plasma frozen within 24 hours for fractionation
- 142 fixed collection sites without blast freezers
- % of plasma units blast frozen unknown

Plasma: Speed of freezing

Issues:

- Blast freezer price: >\$35,000
- Each freezer requires 25 sq. ft. floor space
- # new freezers needed to support peak # units arriving at center--unknown
- Electrical infrastructure upgrades
- Increased breakage/brittleness

ARC Plasma Storage

- 900 freezers, of which 125 are walk-ins, at 48 sites
- Alarms are set at points 5-10°C colder than upper limit of permitted storage range
 - Door openings
 - Defrost cycles

To maintain $< -25^{\circ}\text{C}$

- Alarm set point at $= -30^{\circ}\text{C}$
- Change all 900 freezers from 1-stage to 2-stage compressor systems
- Enhance electrical capacity at almost all sites
- Increase emergency generator capacity at almost all sites
- Consultants, new procedures, validation, training
- Shipping costs double with only $\frac{1}{2}$ # units per box

Collection Type	Annual Units	% AB*
Whole Blood	91.6%	5.6%
Pheresis	8.4%	23.1%
FFP	70.4%	6.5%
24 hour Frozen Plasma	29.6%	8.4%
* % AB in population = 4%		

Product	Collection Type	Annual Units	% AB
FFP	Whole Blood	945,382	4.3%
	Plasma Pheresis	58,237	40.2%
	Plateletpheresis	61,540	8.5%
Subtotal		1,065,159	6.5%
24 Hr Frozen	Whole Blood	439,787	8.4%
	Plasma Pheresis	N/A	N/A
	Platelepheresis	7,344	10.3%
Subtotal		447,131	
Total		1,512,290	7.1%

Suggestion

Adopt ICH temperature range:

Frozen Plasma Storage Conditions

$-20\text{ }^{\circ}\text{C} \pm 5\text{ }^{\circ}\text{C}$

All plasma freezers set the same for:

- To-be-labeled plasma
- Plasma labeled for transfusion
- Plasma labeled for fractionation

History

Plasma derivatives have provided effective therapy to many patients for over 50 years. Historic problems were not related to plasma temperature.

End

Relative Activity (% of time-zero) of coagulation factors

(Time to freezing; Mean \pm 1 SD; N = 10 for each study)

Factor	Study	Holding Temp	8 hr	15 hr	24 hr
Factor V	1	1 – 6 C	98.6 \pm 3.2	102.2 \pm 2.0	101.4 \pm 2.5
	2	4 C	102 \pm 15	N/A	100 \pm 14
Factor VII	2	4 C	97 \pm 21	N/A	92 \pm 20
Factor VIII	2	4 C	84 \pm 16	N/A	64 \pm 13
Factor VIIIC	1	1 – 6 C	89.8 \pm 1.9	80.9 \pm 3.6	75.9 \pm 2.4
Factor IX	1	1 – 6 C	96.5 \pm 9.8	96.8 \pm 5.4	107.2 \pm 6.0
Factor X	2	4 C	99 \pm 14	N/A	99 \pm 13
AT III	2	4 C	95 \pm 6	N/A	95 \pm 7
Von Willebrand Factor antigen	1	1 – 6 C	96.8 \pm 7.6	100.2 \pm 9.0	95.7 \pm 12.5
Ristocetin Cofactor	1	1 – 6 C	103 \pm 18.1	Not done	95.0 \pm 13.2
Protein C	2	4 C	99 \pm 14	N/A	96 \pm 14
Protein S	2	4 C	101 \pm 28	N/A	100 \pm 21
Fibrinogen (in mg/dl)	2	4 C	258 \pm 58	N/A	243 \pm 48 ₂₀

FFP Hemotherapy

COAGULATION FACTOR ACTIVITY

(thawed @ day 0, then refrigerated)

Downes K et al. Transfusion 2001;41;570

	Day 1	Day 2	Day 3	Day 4	Day 5	%change Day 1 to 5	p
VIII	107	76	66	65	65	41	<.05
II	81	81	81	80	80	1	NS
V	70	75	71	68	66	16	NS
VII	90	81	76	72	72	20	NS
X	85	84	84	82	80	6	NS
Fib	225	224	224	224	225	0	NS